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ABSTRACT

National & international granting strategies in PPPM: innovative programmes & economy of personalised medicine

THE INNOVATIVE MEDICINES INITIATIVE - A EUROPEAN PUBLIC-PRIVATE PARTNERSHIP TO BOOST DRUG DEVELOPMENT THROUGH PRECOMPETITIVE RESEARCH

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The pharmaceutical industry is developing new models for drug development based on collaborative efforts and precompetitive research. In order to facilitate the implementation of these new approaches to drug innovation across Europe, the European Union and EFPIA (the European Federation of the Pharmaceutical Industries and Associations) launched the Innovative Medicines Initiative (IMI) in 2008. With a total budget of €2 billion, IMI is the largest public-private partnership (PPP) in life sciences research and development (R&D). To fulfil its mission, IMI implements R&D programmes focused on the development of new tools and methods for the prediction of drug safety or efficacy and more efficient knowledge management. Furthermore, IMI supports education and training projects on the same topics. IMI-sponsored activities are conducted by consortia gathering together pharmaceutical companies, small and medium-sized enterprises (SMEs) and partners from the public sector. EFPIA pharmaceutical companies invest in the form of 'in kind' contributions, while the European Commission provides funding to other consortium members including academic teams, SMEs, patients' organisations, regulatory agencies and other not-for-profit institutions. On the basis of the first achievements of the 23 IMI projects which are currently up and running, we will discuss how precompetitive pharmaceutical research can contribute to shape the future of medicine.

SYSTEMATIC, EVIDENCE-BASED DISCOVERY OF BIOMARKERS AT THE NCI

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Translation of cancer biomarkers into clinically useful diagnostics tests has been plagued by several discovery-related issues, in particular, quality of samples, clinical questions and related study designs. These issues have led to unsatisfactory progress in the translation of biomarkers to clinical use. Most often laboratory discoveries are made using convenience samples and are conducted without due consideration of intended clinical use. There have been numerous published reports pointing out the deficiencies in biomarker research. Over-fitting of the limited data with fewer samples has led to unsubstantiated findings and poor success rates.

In 2000, NCI established a network of investigators comprising basic scientists, epidemiologists, clinicians, and bioinformaticists to address some of the biomarkers developmental issues. The network known as Early Detection Research Network (EDRN; www.cancer.gov/edrn) has emerged as the leading platform supported by the National Cancer institute to systematically discover, develop and validate biomarkers for identifying cancer risk, early cancer detection, and diagnosis and prognosis of cancer.

EDRN has developed a five-phase criterion and a "go" or a "no go", algorithm for selecting biomarkers that are useful. In the five phase criteria, Phase 1 includes exploratory study to identify potentially useful biomarkers. In Phase 2, biomarkers are studied to determine their capacity for distinguishing between cases with cancer and those without. Phase 2 is called the validation phase. Repositories of longitudinally collected clinical specimens from research

cohorts are used in Phase 3 to determine the capacity of a biomarker to detect preclinical disease. Phase 4 consisted of the use of prospective screening studies. Finally, large-scale population studies that evaluate not just the role of the biomarker for detection of cancer, but the overall impact of screening on the population comprises phase 5.
The criteria have been further expanded, especially for Phase II and Phase III, which include: (1) prospective collection of samples from the target population, (2) retrospective random sampling of cases and controls after the outcome status is ascertained. Specimens assayed for biomarkers, are blinded to achieve case-control status. This design is also known as PRoBE design. The PRoBE design has been the basis for EDRN's efforts to collect Reference Samples for quickly and cheaply evaluating biomarkers. The speaker will provide examples of discovery and validation studies based on PRoBE design and reference samples.

INTRODUCTION TO THE ESF FORWARD LOOK ON PERSONALISED MEDICINE

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The European Science Foundation (ESF; www.esf.org) is an independent non-governmental organisation funded by its Member Organisations, European funding and performing organisations as well as scientific academies. The ESF's aim is to act as a catalyst for the development of science by bringing together leading scientists and research funding agencies to debate, plan and implement pan-European initiatives and to explore new directions for research at the European level.
Healthcare is on the brink of a revolution precipitated by dramatic advances in biomedical research. The ability to distinguish, at the molecular level, what makes one person different from another lies at the heart of this fundamental shift. Combined, these developments will change our approach to medicine from finding cures towards individualised prediction, diagnosis, treatment and prevention. Indeed, individualised biological profiles will in the future be used to determine a person's individual healthcare needs. This paradigm shift has been coined as 'personalised medicine'.
The European Medical Research Councils (EMRC), which is the membership organisation for all the medical research councils in Europe under the ESF, has decided to conduct a foresight initiative termed 'Personalised Medicine for the European Citizen'. This field represents an important strategic priority area that involves not only biomedical and technological issues, but also impinges on overarching societal, ethical, economical and legal questions, which is why this Forward Look is supported by all five ESF Standing Committees.
Forward Looks are ESF strategic foresight instruments, intended to enable Europe's scientific community, in interaction with policy makers, to develop medium to long-term views and analysis of future research developments with the aim of defining research agendas at national and European level. The present presentation will introduce the Forward Look instrument and outline the priority areas of this initiative.

THE ECONOMICS OF PERSONALIZED MEDICINE

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Traditional biotechnological or pharmaceutical product development does often not appear to create financial value when average sales figures, attrition rates, and costs are applied to financial models of drug development [1]. Reasons are related to high attrition rates in drug development, high development costs, and limited sales potential due to cost-containment efforts in the healthcare sector. Therefore, biotech companies are not anymore preferred targets for venture capital.
Personalized medicine, apart from the benefits it offers to patients, may raise investors' interest again. Financial models of personalized medicine often predict returns that are in line with investors' expectations who provide the required capital. Historically, big pharma was hesitating to adopt a personalized medicine approach as it was feared that patient stratification would lead to dramatically reduced market sizes. However, there is evidence that personalized drugs, selected based on biomarkers, may show superior effectiveness that warrants premium pricing. It has become common practice in many countries to link reimbursement to cost-effectiveness. Because of its increased effectiveness, many new personalized medicines can be expected to be cost-effective even when assuming premium prices.

Using a hypothetical case example of a highly effective personalized renal cell cancer therapy, it was calculated that

- Phase III development costs may be reduced by more than 30%,
- Phase III development time may be reduced (depending on recruitment time for a stratified patient group),
- the financial value for a personalized drug treatment may increase by over 60% for a pharma company and by over 50% for a biotech when one accounts for decreased development cost and time, compared to 'typical' drug development,[1]
- the financial value may increase by more than 140% for pharma and more than 110% for biotech if, in addition, higher success probabilities are assumed for Phase III and approval.[2]

Although cost-effective, new personalized medicines may raise overall healthcare spending in the long-run. Society needs to develop new compensation models to ensure that every patient in need can benefit from new personalized therapies.

Reference

1. Nickisch KJ, Greuel JM, Bode-Greuel K. How can pharmaceutical and biotechnology companies maintain a high profitability? J. Commercial Biotechnology. 2009;15:309–323.

[1] Assumptions renal cell cancer: market size: 45,000 pts.; biomarker-positive: 9,000 pts.; price of standard therapy: $30,000.-; price of cost-effective personalized therapy: $90,000; peak patient share: 60%, development costs: preclinical:$8 m, Ph.I:$8 m, Ph.IIa:$12 m, Ph.IIb:$25 m, Ph.III:$90 m traditional drug development, Ph.III personalized medicine:$60 m; Ph.III duration traditional DD: 3 years, Ph.III PM: 2 years; COGS: 8% of sales; MKTG: $200 m close to launch, then 30% of sales; success probabilities: preclinical: 60%, Ph.I: 67%, Ph.IIa: 50%, Ph.IIb: 75%, Ph.III: 70%, approval: 80%; cost of capital: pharma: 10%, biotech: 18%; perspective: preclinical development.

[2] Assumed success probabilities: Ph.III: 80%, approval: 90%.

ECONOMIC CONCERNS ABOUT GLOBAL HEALTHCARE: MEETING THE ECONOMIC CHALLENGE OF PREDICTIVE, PREVENTIVE, AND PERSONALISED MEDICINE

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The introduction of biological science into the practice of medicine at the end of the 20th century was a big transforming event for the profession, leading to different new medical models such as predictive, preventive, and personalised medicine. Each of them is a rapidly emerging field that helps us to determine the individual risk to develop specific diseases, detect the disease's earliest onset, to prevent diseases or intervene early enough to provide maximum benefit for each patient. This contribution describes the different economic aspects of prospectively medicine, the economic components of a predictive, preventive and personalised health plan, and shows how prospective care could relate to the community in order to prevent possible collapse of healthcare systems in the future. Further more there is an urgently need in multidisciplinary approaches to develop innovative applications of new biopharmaceutical- and diagnostic technologies and to appropriate delivery models. Pilot programmes to support prospective healthcare have already been set in motion and European initiative, such as EPMA, develop a new paradigm to use innovative diagnostic models in prospective medicine. Political support will also be needed to help for achieving rational reimbursement between providers and payers, so that prospective care can fulfil its promise of being the cost-effective medical model to improve national health systems.